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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/777,542	02/12/2004	Unchalee Kositprapa	141-446	5119

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EXAMINER	
WEDDINGTON, KEVIN E	

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1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/777,542	KOSITPRAPA ET AL.	
	Examiner	Art Unit	
	Kevin E. Weddington	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5-18-04; 3-3-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-34 are presented for examination.

Applicants' preliminary amendment filed May 22, 2006 and the information disclosure statements filed May 18, 2004 and March 3, 2006 have been received and entered.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-31 of copending Application No. 10/664,803. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present application teaches a pharmaceutical dosage form comprising a first and second active drug wherein the agents are antihyperglycemic compounds and

thiazolidinediones and are released at the various T_{max}, and the copending application teaches a pharmaceutical controlled release dosage form comprising a first and second active drug wherein the agents are biguanides and thiazolidinediones and released at the same T_{max}. The present application encompasses the copending application's first and second active drugs since biguanides are antihyperglycemic.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-34 are not allowed.

Claims 1-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-38 of copending Application No. 11/094,493. Although the conflicting claims are not identical, they are not patentably distinct from each other because both copending applications describe a controlled release dosage form comprising first and second active agents wherein the agents are antihyperglycemic drugs and thiazolidionediones and are released at the same T_{max}.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-34 are not allowed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled

in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a written description rejection.

Claims 1-34 described compounds that are antihyperglycemic drugs and thiazolidionedione derivatives. The instant claims cover all compounds having the pharmaceutical property of being an antihyperglycemic drug and a thiazolidionedione derivative to treat type II diabetes. Describing a compound by its functions will not substitute for written description of the structure of the compound. The invention should be described in such a way as to described what the invention is, not what the invention does. Describing the function of a compound fails to distinguish the compound from other molecules or agents that can perform the same functions.

Undue experimentation is a conclusion reaches by weighing the noted factual considerations set forth below as seen in In re Wands, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1401 (Fed. Cir. 1988). A conclusion of lack of enablement means that, based on the evidence regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

The factors include:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice that instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

Claims 1-34 are directed to compounds that are antihyperglycemic drugs and thiazolidionedione derivatives that are used to treat type II diabetes. The instant claims cover all compounds having pharmaceutical property of being known as a compound (antihyperglycemic drugs and thiazolidionedione derivatives) to treat type II diabetes. Although claims 21, 22, 29 and 30 lists specific examples of compounds which are alleged to have the property to treat type II diabetes, and claims 1-20, 23-28 and 31-34 are directed to a variety of compounds with the functional description of

being known as a compound which is alleged to have the property to treat type II diabetes.

The instant claims are very broad. For instance, claims 1-20, 23-28 and 31-34 are to a plethora of compounds of as described by the functional properties as being known to treat type II diabetes.

The relative skill of those in the art is generally that of a Ph.D. or M.D.

One skilled in the art would not predict from the instant disclosure which compounds would fall under the umbrella of functional description of being known as broadly as an antihyperglycemic drug and a thiazolidionedione derivatives. In fact, the courts have made a distinction between mechanical elements function the same in different circumstances, yielding predictable results, chemical and biological compounds often react unpredictably under different circumstances.

Note, the two state of the prior art references, Answers.com, show the various biguanides such as phenformin and buformin were withdrawn from the market due to toxic effects; and the MedicineNet.com shows the thiazolidinedione such as troglitazone was taken off the market because of liver toxicity.

The breadth of the claims

The claims are very broad and inclusive to all antihyperglycemic drugs and thiazolidionedione derivatives that are used to treat type II diabetes.

The amount of direction or guidance provided and the presence or absence of working examples

The working examples are limited to the combination of metformin (the biguanide) and pioglitazone (the thiazolidinedione derivative).

No examples showing the other biguanides such as pheformin and buformin that were withdrawn from the market due to toxic effects in combination with troglitazone (a withdrawn from the market also).

The quantity of experimentation necessary

Applicants have failed to provide guidance as to how the skilled artisan would be able to extrapolate from the disclosure and examples provided to make and possibly use the claimed invention. The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. (In re Fischer, 427 F. 2d 839, 166 USPQ 24; Ex Parte Hitzeman, 9 USPQ 2d 1823).

The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in the determining whether "undue experimentation" is required to make and use the instant invention. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if its is merely routine, or of the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. For these reasons, one of ordinary skill in the art would be burdened with

undue "painstaking experimentation study" to determine all the compounds or agents that are broadly known to possess the property of treating type II diabetes as described in this specification. In view of the information set forth supra, the instant disclosure is not seen to be sufficient to describe the use of any compound , which is regarded as the functional description of a compound (antihyperglycemic drugs and thiazolidionedione derivatives) for treating type II diabetes.

Therefore, undue experimentation would be required to practice the invention as it is claimed in its current scope.

Claims 1-34 are not allowed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vergez et al. (US 2006/0204578 A1).

Vergez et al. teach a controlled release osmotic dosage form comprising two different active agents, i.e., to different antidiabetic agents such as biguanides and thiazolidinediones, wherein the dosage form comprises a membrane surrounding a bilayered core, and the core comprising an inner nucleus comprising the first active agent and a second layer surrounding the inner nucleus comprising a different second active agent. At **[0043]** and **[0063]**, Vergez et al. explicitly teaches an optional embodiment wherein the tablet comprises an external coating disposed on the outside of the osmotic device comprising one or more active agents for immediate delivery to the environment of use. Further at **[0149]** and claim 50, Vergez et al. teaches that antidiabetic agents include thiazolidinediones such as rosiglitazone, pioglitazone and troglitazone and biguanides such as metformin. The synergistic effect of biguandine and thiazolidinedione for treating diabetes and diabetic conditions is well-known in

the art. According to the *Physician's Desk Reference*, effective dosage amounts of a thiazolidinedione such as pioglitazone are known to be 15, 30 and 45 mg. The effective dosage for a biguanide such as metformin is known to range from 500 to 2550 mg. One of ordinary skill in the art at the time of the invention would have been motivated to include the antidiabetic with the smaller dosage (lower MW) in the outer layer since it is intended for immediate release and has a quicker dissolution profile. Likewise, the artisan would have been motivated to include the larger dosage (higher MW) antidiabetic in the core since it has slower dissolution profile and would take longer for it to erode or dissolve.

Vergez et al. teach the various limitations of the instant claims with regard to the features such as the antihyperglycemic drug, binding agent, absorption enhancer, lubricant, seal coat, semipermable membrane, polymer, flux enhancer, plasticizer, surfactant, pore-forming agents, and passageways at **[0104-0109, 0121, 0122, 0126, 0133, 0134]**.

Vergez et al. does not teach the % as claimed in the instant application. However, these percentages can be obtained through routine experimentation. The artisan would have been motivated to determine these amounts to get the maximum efficacy of the dosage form. Results obtainable through routine experimentation are not patentable over the art.

Vergez et al. teach the relative amounts of each active agent released at a given time can be controlled by changing the location of the passageway(s) in the wall(3). For example, if the first (4) and second (6) compositions have the same

release properties and the device includes the sole passageway (50 centered on the composition (4) before it releases any of the composition (6). If the first (4) and second (6) composition have the same release properties and the device includes the sole passageway (5) in communication with the composition (4) and proximal but not in direct communication with the composition (6), the device (1) will release only a minor portion of the first composition (4) by the time it begins to release the second composition (6) (see **[0069]**).

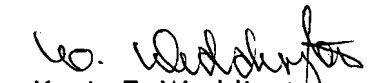
Vergez et al. teach in particular embodiment that the controlled release dosage form will provide effective amounts of active agent for a period of not less than 18 hours and not more that 30 hours, or not less than 20 hours and not more than 28 hours, or not less than 22 hours and not more that 24 hours. Vergez et al. further teach that the artisan of ordinary skill will understand that administration of a single unit dose period of time may be insufficient to maintain therapeutic plasma levels of active agent for up to 24-30 hours and that multiple unit doses administered over an equal number of days may be required to maintain therapeutic plasma levels of active agent for up to 24-30 hours. The determination of the time release quantities in claims is well within the level of one of ordinary skill in the art. The artisan would have been motivated at the tile of the inventions to determine the maximum release times to determine optimum efficacy of the drugs being administered.

Claims 1-34 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin E. Weddington whose telephone number is (571)272-0587. The examiner can normally be reached on 12:30 pm-9:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Kevin E. Weddington
Primary Examiner
Art Unit 1614

K. Weddington
June 6, 2007